

82

Uitra

09/549463

=> fil medl,hcaplus,biosis,embase,jicst,wpids
COST IN U.S. DOLLARS

SINCE FILE
ENTRY
0.21

TOTAL
SESSION
0.21

FULL ESTIMATED COST

FILE 'MEDLINE' ENTERED AT 15:44:56 ON 03 JUN 2002

FILE 'HCAPLUS' ENTERED AT 15:44:56 ON 03 JUN 2002
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=> s (adenovir? ela or e1a or e1a protein or antigen?(a)viral(a)(tumor or tumour)
or oncogene?(a)protein?(a)viral or transcript? factor? or adenovir? early protein?)

L1 71389 FILE MEDLINE
L2 78951 FILE HCAPLUS
L3 49061 FILE BIOSIS
L4 44344 FILE EMBASE
L5 7321 FILE JICST-EPLUS
L6 1209 FILE WPIDS

TOTAL FOR ALL FILES

L7 252275 (ADENOVIR? E1A OR E1A OR E1A PROTEIN OR ANTIGEN?(A) VIRAL(A) (TUM
OR OR TUMOUR) OR ONCOGENE?(A) PROTEIN?(A) VIRAL OR TRANSCRIPT?
FACTOR? OR ADENOVIR? EARLY PROTEIN?)

=> s elb or e2a

L8 1363 FILE MEDLINE
L9 1728 FILE HCAPLUS
L10 1396 FILE BIOSIS
L11 1156 FILE EMBASE
L12 56 FILE JICST-EPLUS
L13 177 FILE WPIDS

TOTAL FOR ALL FILES

L14 5876 E1B OR E2A

=> s (l7 or l14) and (eukaryo? or mammal? or human)(a)cell!

L15 2055 FILE MEDLINE
L16 2420 FILE HCAPLUS
L17 1375 FILE BIOSIS
L18 1237 FILE EMBASE
L19 43 FILE JICST-EPLUS
L20 131 FILE WPIDS

TOTAL FOR ALL FILES

L21 7261 (L7 OR L14) AND (EUKARYO? OR MAMMAL? OR HUMAN) (A) CELL!

=> s l21 and (erythropoietin? or glycoprotein hormone? or
receptor?(a)erythropoietin? or anemia disease or erythropoiesis)

Searched by: Mary Hale 308-4258 CM-1 12D16

L22 15 FILE MEDLINE
 L23 35 FILE HCAPLUS
 L24 11 FILE BIOSIS
 L25 14 FILE EMBASE
 L26 0 FILE JICST-EPLUS
 L27 4 FILE WPIDS

TOTAL FOR ALL FILES

L28 79 L21 AND (ERYTHROPOIETIN? OR GLYCOPROTEIN HORMONE? OR RECEPTOR?(A
) ERYTHROPOIETIN? OR ANEMIA DISEASE OR ERYTHROPOIESIS)

=> s l28 and ((post or peri)(a)(modif? or transl?) or posttransl? or peritransl?)

L29 0 FILE MEDLINE
 L30 1 FILE HCAPLUS
 L31 0 FILE BIOSIS
 L32 0 FILE EMBASE
 L33 0 FILE JICST-EPLUS
 L34 1 FILE WPIDS

TOTAL FOR ALL FILES

L35 2 L28 AND ((POST OR PERI)(A)(MODIF? OR TRANSL?) OR POSTTRANSL? OR
 PERITRANSL?)

=> dup rem l35

PROCESSING COMPLETED FOR L35

L36 2 DUP REM L35 (0 DUPLICATES REMOVED)

=> d cbib abs 1-2

L36 ANSWER 1 OF 2 WPIDS (C) 2002 THOMSON DERWENT

AN 2000-665247 [64] WPIDS

AB WO 200063403 A UPAB: 20001209

NOVELTY - A method (M1) of producing recombinant proteins in a eukaryotic cell, preferably a human cell line, which comprises a sequence encoding at least one E1 protein of an adenovirus or its functional homologue, fragment or derivative, is new. The cell does not encode a structural adenoviral protein from its genome or from a sequence integrated into the genome.

DETAILED DESCRIPTION - A method (M2) of producing recombinant proteins in a eukaryotic cell, preferably a human cell line, which comprises a sequence encoding at least one E1 protein of an adenovirus or its functional homologue, fragment or derivative, is new. The cell does not encode a structural adenoviral protein from its genome or from a sequence integrated into the genome.

The method comprises providing the cell with a gene encoding a recombinant protein, culturing the cell in a suitable medium and harvesting the protein substance from the cell and/or medium.

INDEPENDENT CLAIMS are also included for the following:

(1) a method (M2) for enhancing production of a recombinant protein in a eukaryotic cell, comprising providing a eukaryotic cell with a nucleic acid encoding at least part of the protein, where the coding sequence is under control of a Cytomegalovirus (CMV) promoter, an **E1A** promoter, or their functional homologues, derivatives and/or fragments and further providing the cell with an **E1A** activity or **E1A**-like activity;

(2) a recombinant mammalian cell immortalized by the presence of at least one adenoviral E1 protein or its functional derivative, homologue and/or fragment, and further comprising a nucleic acid (N1) in a functional format for expressing at least one variable domain of an immunoglobulin or its functional derivative, homologue and/or fragment;

(3) a method (M3) for producing at least one variable domain of an immunoglobulin, comprising culturing the recombinant mammalian cell of

(2);

(4) an immunoglobulin or its functional part, homologue and/or derivative, obtainable by the method of (M3);

(5) a recombinant protein obtained by the method of M1, M2 or M3, where the recombinant protein has a human glycosylation pattern different from the isolated natural counterpart protein;

(6) a recombinant **erythropoietin** molecule obtained by the method of M1 or M2;

(7) a human cell having a genomic sequence encoding at least one E1 protein of an adenovirus or its functional derivative, homologue or fragment, where the cell does not produce structural adenoviral proteins and has a gene encoding a recombinant protein; and

(8) a viral protein obtained by the method of M1 or M2, where the viral protein is free from any non-human mammalian proteinaceous material.

ACTIVITY - None given.

No biological data given.

MECHANISM OF ACTION - Vaccine.

No biological data given.

USE - The recombinant **mammalian cells** are useful for producing variable domains of an immunoglobulin which have **post-translational** modifications different than that of their isolated natural counterparts. The **human cells** having a genomic sequence encoding at least one E1 protein of an adenovirus or its functional derivative, homologue or fragment are useful for the production of a recombinant protein, e.g. a viral protein for use in a vaccine. The adenoviral **E1B** protein or its functional derivative, homologue and/or fragment has anti-apoptotic activity and is useful for enhancing the production of a proteinaceous substance in a eukaryotic cell (all claimed).

ADVANTAGE - The cell is capable of producing 2 to 200 fold more recombinant protein and/or proteinaceous substances than conventional mammalian lines such as Chinese Hamster Ovary (CHO), COS cells, vero, Hela, BHK or Sp-2 cell lines. Specifically, the human cell is capable of producing in excess of 100, preferably 5000, units **erythropoietin** /million cells in 24 hours (claimed).

Dwg.0/24

L36 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2002 ACS

1999:457101 Document No. 132:47942 Regulation of cellular 15-lipoxygenase activity on pretranslational, translational, and **posttranslational** levels. Kuhn, Hartmut; Heydeck, Dagmar; Brinckman, Roland; Trebus, Frank (Institute of Biochemistry, University Clinics Charite, Humboldt University, Berlin, D-10115, Germany). Lipids, 34(Suppl., Fatty Acids and Lipids from Cell Biology to Human Diseases), S273-S279 (English) 1999. CODEN: LPDSAP. ISSN: 0024-4201. Publisher: AOCs Press.

AB A review with 34 refs. with an emphasis on the author's results. In **mammalian cells**, enzymic lipid peroxidn. catalyzed by 12/15-lipoxygenases is regulated by pretranslational, translational, and **posttranslational** processes. In rabbits, rats, and mice induction of exptl. anemia leads to a systemic up-regulation of 12/15-lipoxygenases expression. In addn., interleukins-4 and -13 were identified as strong up-regulators of this enzyme in human and murine monocyte/macrophages and in the lung carcinoma cell line A549, and the interleukin-4(13) cell surface receptor as well as the signal transducer and activator of transcription 6 (STAT6) appears to be involved in the signal transduction cascade. On the level of translation, 15-lipoxygenase synthesis is blocked by the binding of regulatory proteins to a characteristic guanine-cytosine-rich repetitive element in the 3'-untranslated region of the rabbit 15-lipoxygenase mRNA, and the formation of such 15-lipoxygenase mRNA/protein complexes was identified as mol. reason for the translational inactivity of the 15-lipoxygenase mRNA in immature red blood cells. However, proteolytic breakdown of the regulatory proteins which were

recently identified as hnRNP K and hnRNP E1 overcomes translational inhibition during later stages of reticulocyte maturation. For maximal intracellular activity, 12/15-lipoxygenases require a rise in cytosolic calcium concn. inducing a translocation of the enzyme from the cytosol to cellular membranes as well as small amts. of preformed hydroperoxides which act as essential activators of the enzymes. 12/15-Lipoxygenases undergo irreversible suicide inactivation during fatty acid oxygenation, and this process may be considered an element of down-regulation of enzyme activity. Suicide inactivation and proteolytic breakdown may contribute to the disappearance of functional 12/15-lipoxygenase at later stages of erythropoiesis.

=> log y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

27.16

27.37

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

-0.62

-0.62

STN INTERNATIONAL LOGOFF AT 15:56:39 ON 03 JUN 2002